

**REMARKS**

Claims 1-21 are currently pending in the application. Claims 18-21 have been canceled as drawn to a non-elected invention. Claim 9 has also been canceled.

Claims 1, 2, 4-6, 8, 11-13 and 17 have been amended. New claims 22-25 have been added. Support for the new claims may be found, for example, in Figures 11, 12, 14 and 15 of the specification and related examples.

**Objection to the Title**

The title has been objected to because it is allegedly not descriptive. Applicants have amended the specification to include a new title. Applicants respectfully request withdrawal of the objection to the title.

**Claim Objections**

Claim 2 has been objected to because the Examiner alleges the conjunction “or” should be used when listing the species. Applicants have amended claim 2 accordingly.

Claim 8 has been objected to because the claim recites “the methods” of claim 1. Applicants have amended claim 8 to recite “method”.

Applicants respectfully request withdrawal of the claim objections.

**Claim Rejections – 35 U.S.C. § 112, second paragraph**

Claims 1 through 17 have been rejected under 35 U.S.C. § 112, second paragraph.

Claim 1 is rejected because it is allegedly missing a contact step that would give an indication of how ORP150 is detected in the bodily fluid sample. Applicants have amended claim 1 to render this rejection moot.

In claims 5-6, the term “the immunoassay” allegedly lacks antecedent basis in claim 1. Applicants have amended claims 5-6 to correct the antecedent basis.

In claim 7, the term “the antibody” allegedly lacks antecedent basis in claim 1. Applicants submit that amended claim 1 now includes the term “antibody” and therefore there is proper antecedent basis for the term in claim 7.

In claims 12-13, the term “the immunoassay” allegedly lacks antecedent basis in claim 8. Applicants have amended claims 12-13 to correct the antecedent basis.

Claims 4-6 and 11-13 allegedly provide for using an immunoassay but do not set forth any steps involved in the method. Applicants submit that the amendments to claims 4 and 11 obviate this rejection.

Claims 8 and 11-17 are directed to detection of a second marker for which there is allegedly no support in the specification. Claim 8 has been amended to limit the second marker to a natriuretic peptide

Accordingly, Applicants request the reconsideration and withdrawal of the rejections for indefiniteness.

*Claim Rejections – 35 U.S.C. § 112, first paragraph - written description*

Claims 1 through 17 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Specifically, claim 1 has been rejected as being drawn to a genus of polypeptides that is defined only by name. Applicants have amended claim 1 to render this rejection moot.

Claims 9 and 10 have also been rejected as being drawn to a genus of polypeptides that is defined only by name.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was “ready for patenting” such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

Claim 9 has been canceled. However, inasmuch as the term “natriuretic peptide” appears in other claims, although the specification does not provide sequences for the natriuretic peptide species described therein, the Applicants have provided publication citations for the natriuretic peptide species that are incorporated by reference in their entireties, which provide adequate description and sufficient detail about the natriuretic peptide species, e.g., on page 1, third

paragraph, page 10, first paragraph, etc. Further, as regards claim 10 and its recitation of BNP and N-BNP, Applicants have reduced to practice at least one assay incorporating the use of N-BNP as described in Examples 1 and 2. Thus, Applicants have demonstrated possession of multiple species of the claimed natriuretic peptide genus and BNP and N-BNP species.

Accordingly, Applicants request the reconsideration and withdrawal of the rejections for lack of written description.

*Claim Rejections – 35 U.S.C. § 112, first paragraph - enablement*

Claims 1 through 17 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

Specifically, claim 1 has been rejected as not enabled by the specification for detecting any ORP150 protein. Applicants have amended claim 1, thus rendering the rejection moot.

Claim 8 has been rejected as not providing enablement for detecting any second marker protein. Applicants have amended claim 8 to remove the term “second marker”, thus rendering the rejection moot.

Claim 9 has been rejected as not providing enablement for detecting any natriuretic polypeptide. Applicants have canceled claim 9, but amended claim 8 now recites the term “natriuretic polypeptide.” The Examiner argues that the method of detection in claim 8 is not limited to the bodily fluid sample of claim 1. Applicants have amended claim 8 to required that the natriuretic polypeptide be detected in the bodily fluid sample. Claim 8 as amended is enabled by the specification. The specification provides extensive description of natriuretic polypeptides and methods of assaying them, along with two working examples wherein ORP150 and a natriuretic polypeptide are used together in assays for various heart diseases.

Accordingly, Applicants request the reconsideration and withdrawal of the rejections for lack of enablement.

*Claim Rejections – 35 U.S.C. § 103*

Claims 1-4, 7-11 and 14-17 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,948,637 in view of Hall et al.

The ‘637 patent does not teach or suggest a method for detecting tissue hypoxia in a mammalian subject by contacting a bodily fluid sample with an antibody specific for an oxygen

related protein 150 (ORP150) comprising SEQ ID NO: 2 or an immunoreactive fragment thereof in order to detect the level of ORP150 in the bodily fluid sample, whereby an elevated level of ORP150 relative to normal is indicative of an increased risk of heart disease. Hall is relied on by the Examiner as teaching the detection of natriuretic peptide, particularly in combination with other diagnostic tests.

One of skill in the art would not have been motivated to turn to the teachings of Hall to remedy the deficiency of the '637 patent disclosure in regard to claims 1-4 and 7. Hall relates to detection of natriuretic peptides alone and in combination with other diagnostics. Claim 1 and its dependent claims 2-4 and 7, however, only relate to the detection of ORP150. One of skill in the art would have not turned to literature regarding detection of natriuretic peptides to determine how to adapt an assay for ORP150 detection in bodily fluids. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.

With regard to claims 8-11 and 14-17, Applicants respectfully assert that the Examiner has misconstrued the teachings of Hall. Hall discusses in section 7 whether the natriuretic peptide measurements would make other diagnostic examinations superfluous and discusses whether the natriuretic peptide measurements could replace the existing gold standard or only be used to supplement current methods. Thus, it does not teach or suggest the desirability of combining the natriuretic peptide measurements with *any* other diagnostic that might be developed later on. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. Applicants respectfully submit that based on the teachings of Hall, one of skill in the art would not have been motivated to combine a completely novel diagnostic based on another protein as taught in the '637 patent.

Thus, Applicants respectfully request reconsideration and withdrawal of the rejection for obviousness over U.S. Patent No. 5,948,637 in view of Hall et al.

Claims 4-5 and 11-12 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of Karl et al.

As discussed above, the combination of the '637 patent with Hall does not render claims 1-4, 7-11 and 14-17 obvious. The addition of Karl et al does not remedy this deficiency.

Thus, Applicants respectfully request reconsideration and withdrawal of the rejection for obviousness over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of Karl et al.

Claims 4, 6, 11 and 13 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of May et al.

As discussed above, the combination of the '637 patent with Hall does not render claims 1-4, 7-11 and 14-17 obvious. The addition of May et al does not remedy this deficiency.

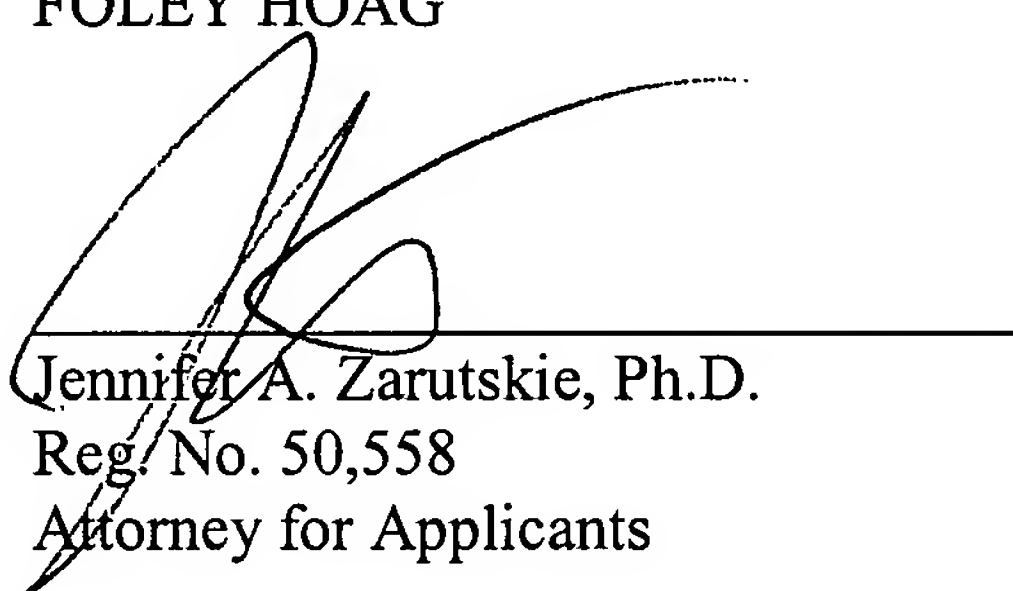
Thus, Applicants respectfully request reconsideration and withdrawal of the rejection for obviousness over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of May et al.

**CONCLUSION**

Early and favorable consideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000.

Respectfully submitted,  
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